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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,214	07/09/2001	Gordon L. Amidon	PSL-10202/39	6240

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EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 07/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/901,214	Applicant(s) AMIDON ET AL.	
	Examiner San-ming Hui	Art Unit 1617	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *15-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment of claims 1, 11, and 12 filed April 2, 2002 is acknowledged

Newly submitted claims 15-20 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 15-20 are directed to a method preparing a pharmaceutical delivery vehicle. The originally filed claims 1-14 are directed to a pharmaceutical vehicle. They are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the pharmaceutical delivery vehicle can be prepared by a different process such as mixing the matrix materials together, then adding the drug particles and subsequently removing the solvent.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 15-20 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

The outstanding rejections of claims 1-14 under 35 USC 112, first and second paragraph are withdrawn in view of the amendments filed April 2, 2002.

Claim Rejections - 35 USC § 112

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "the ratio of the initial mass of ... being such that the drug particle is solubilized to... greater than 0.001 millgram per milliliter" in claims 1 and 12 renders the claims indefinite as to the ratio encompassed by the claims. It is not clear to one of ordinary skill in the art what ratio it would be referring.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,2, 5, 6, and 8-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Amidon et al. (US Patent 5,834,022).

Amidon et al. teaches a coating (the boundary layer) composition consisting essentially of gelatin (a matrix) and lecithin (solubilizing agent) and in which the drug are disposed within the boundarylayer (See particularly col. 9, line 15 – col. 12, line 19). Amidon et al. also teaches cyclosporin and griseofluvin (the drug actives) have dissolution rates of both drugs increased to about 20% and 40% respectively when employed the lecithin/gelatin coating drug delivery system (See particularly col. 6, lines 3-13; also Figures 2-7).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 4, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amidon et al. (US Patent 5,834,022) in view of Woo (US Patent 5,589,455) and Gennaro et al. (Remington's Pharmaceutical Sciences, 18th ed., 1990, page 1662-1664).

Amidon et al. teaches a coating (the boundary layer) composition consisting essentially of gelatin (a matrix) and lecithin (solubilizing agent) and in which the drug are disposed within the boundary layer (See particularly col. 9, line 15 – col. 12, line 19). Amidon et al. also teaches cyclosporin and griseofluvin (the drug actives) have dissolution rates of both drugs increased to about 20% and 40% respectively when employed the lecithin/gelatin coating drug delivery system (See particularly col. 6, lines 3-13; also Figures 2-7).

Amidon et al. does not expressly teach that the coating composition contains emulsion or microemulsion. Amidon et al. does not expressly teach that the matrix that formed the boundary layer comprises a film.

Woo teaches that a microemulsion may be used in a soft capsule pharmaceutical formulation to enhance the solubility of a poorly soluble drug, cyclosporin (See particularly abstract, also 4, line 53 to col. 7, line 13).

Gennaro et al. teaches that a gelatin film may be used in the preparation of soft gelatin capsules (See particularly page 1663, col. 2, second paragraph).

It would have been obvious to one skill in the art when the invention was made to incorporate microemulsion and the film into the composition of Amidon et al.

One of ordinary skill in the art would have motivated to incorporate microemulsion and the film into the composition of Amidon et al. because both microemulsion and the film are well known in the art to be useful in poorly-soluble enhancement formulation, based on Woo and Gennaro et al. Therefore, absent evidence to the contrary, combining agents which are known to be useful to enhance drug solubility individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, the experiment

examples disclosed in page 16-18 and Figures 3-4 of the instant specification have been considered, but are not found persuasive. It is unclear what drug actives are studied in the instant experiment. Therefore, it is impossible to evaluate and compare the data for unexpected results. No clear and convincing unexpected results are seen herein.

Response to Arguments

Applicant's arguments filed April 2, 2002 averring Amidon et al.'s failure to teach the relationship between the mass of the drug particle and the volume of the diffusional boundary layer in solubilizing the drug particle have been fully considered but they are not persuasive. Amidon et al. clearly teaches the ratio of lecithin and gelatin in the examples disclosed in col. 9, line 15-col. 12, line 19 as 1:1 ratio (1 gram of lecithin to 1 gram of gelatin). Amidon et al. also teaches this particular ratio can solubilize a poorly soluble drug: cyclosporin. Amidon et al. does teach the relationship between the mass of the drug particle and the volume of the diffusional boundary layer in solubilizing the drug particle. Therefore, Amidon et al. still anticipates the instant invention.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

RUSSEL TRAVERS
PRIMARY EXAMINER
GROUP 1200

San-ming Hui
June 27, 2002